Remarks

Upon entry of this amendment, claims 95-112 will be pending in the above-captioned application. Claims 95-97 have been amended to recite "wherein said polypeptide stimulates proliferation of epithelial cells." Support for this amendment is found in the specification as filed and, for example, at original claim 37.

Claims 96 and 97 have been rewritten in independent form. Claims 98-102 have been amended to single dependency. Claims 99-112 have been added to claim the subject matter that had been deleted by the amendment of claims 98-102 to single dependent form.

Accordingly, no new matter has been introduced and entry of this amendment is respectfully solicited.

I. Written Description Rejections

The Examiner has rejected claims 95-102 under 35 U.S.C. § 112, first paragraph for alleged lack of written description. In particular, the Examiner contends that

> ...the only factor present in the claim is a partial structure in the form of percent identity. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus. ... As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity of simplicity of the method of isolation.

See, Office Action, page 3.

Applicants respectfully disagree and traverse. Applicants have amended claims 95-97 to recite "wherein said polypeptide stimulates proliferation of epithelial cells." For the reasons developed below, Applicants believe that the claims, both as amended and as rejected, are fully described in the instant application.

The test for the written description requirement is whether one skilled in the art could reasonably conclude that the inventor has possession of the claimed invention in the specification as filed. (*See*, M.P.E.P. § 2163(I) at 2100-15, and *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991)).

The Federal Circuit has re-emphasized the well-settled principle of law that "[t]he written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary

skill in the art to recognize that [he or she] invented what is claimed,"' *Union Oil Company of California v. Atlantic Richfield Company*, 208 F.3d 989, 54 U.S.PQ.2d 1227 (Fed. Cir. 2000). Further, the Federal Circuit has emphasized the importance of what the person of ordinary skill in the art would understand from reading the specification; and not whether the specific embodiments had been explicitly described or exemplified. Indeed, the court noted that "the issue is whether one of skill in the art could derive the claimed ranges from the patent's disclosure." *Union Oil Company of California v. Atlantic Richfield Company*, 208 F.3d at 1001, (emphasis added).

Thus, the Examiner bears the initial burden of presenting a *prima facie* case of unpatentability based on lack of written description by presenting evidence or reasons why one skilled in the art would *not* reasonably conclude that Applicants possessed the subject matter as of the priority date of the present application. *In re Wertheim*, 541 F.2d 257, 262, 191 USPQ2d 90, 96 (C.C.P.A. 1976); M.P.E.P. § 2163.04. In the instant case, the Examiner has not met this burden because the specification describes with reasonable clarity to one of skill in the art that the inventors were in possession of the claimed invention on the earliest filing date of the present application.

In particular, Applicants submit that the specification provides ample written description to enable one of skill in the art to visualize or recognize the identity of the members of the claimed genus. For example, the specification provides the skilled artisan with the detailed structure of the polypeptides of the invention, *e.g.*, the amino acid sequence of the N-terminal deletion mutant Ala (63) - Ser (208) of SEQ ID NO:2, herein referred to as KGF-2Δ28. *See*, for example, specification at page 16, lines 1 to 3; at page 46, lines 1-3; and at Figure 26.

In addition to the amino acid sequence common to the polypeptides of the claimed invention (e.g., KGF-2Δ28), the specification further provides ample disclosure of other relevant characteristics of the claimed polypeptides. First, the specification provides the parameters used to determine the percent identity of the polypeptides of the claimed invention. *See*, for example, specification at page 36, line 10 to page 37, line 25. The specification further provides a detailed analysis of the structural attributes of the KGF-2 protein, including preferred amino acid substitutions and point mutations, many of which are encompassed within the scope of the claims. *See*, for example, specification at page 11, line 22 to page 12, line 3; at page 29, line 28 to page 30, line 30; at page 35, lines 3-19;

page 50, line 26 to page 53, line 3; and at Figure 4A-4E. Moreover, the specification provides specific N-terminal and C-terminal deletion mutants of SEQ ID NO:2, for example, Ser (69) - Ser (208), which fall within the scope of the instant invention. *See*, specification, for example, at page 16, lines 1-6; at page 44, line 27 to page 50, line 2.

The specification also provides a detailed analysis of the functional attributes of the KGF-2 protein, such as, for example, antigenic index of the KGF-2 polypeptide. *See*, specification, for example, at page 11, line 22 to page 12, line 3, and at Figure 4A-4E. In particular, the specification discloses specific antigenic and hydrophilic regions of the KGF-2 protein. *See*, specification, for example, at page 40, lines 7-16; page 53, line 20 to page 54, line 9; and at Figure 4A-4E. Many of these antigenic and hydrophilic regions completely fall within the amino acid sequence of KGF-2Δ28. The specification further teaches the use of the polypeptides of the invention, including the polypeptides with percent identity to KGF-2Δ28, for generating antibodies that specifically bind a polypeptide of SEQ ID NO:2. *See*, specification, for example, at page 39, lines 5-10; at page 41, lines 8-11; and at page 66, line 18 to page 67, line 1.

Accordingly, one skilled in the art, enlightened by teachings of the present application, could readily envision countless polypeptide sequences that comprise the specified polypeptides. For example, the skilled artisan could clearly envision each of the polypeptides that are 90% identical to KGF-2Δ28 as a polypeptide with at least 1, 2, 3, 4, etc. amino acid substitutions or deletions along its length. Indeed, nothing more than a basic knowledge of the genetic code and what is described in the specification would be required for the skilled artisan to identify every single one of the polypeptides that are 90% identical to KGF-2Δ28. Clearly, such knowledge is well within what is expected of the skilled artisan.

Thus, the instant claims clearly distinguish the boundaries of each claimed genus and identify all of the members of each genus. Accordingly, one skilled in the art would reasonably conclude that Applicants had possession of the polypeptides encompassed by the rejected claims, upon reading the present application as filed.

Accordingly, from reading the specification, the skilled person would immediately recognize that, at the time the specification was filed, the Applicants had "invented what is claimed" (*Vas-Cath*, 935 F.2d at 1563); namely, a genus of proteins comprising polypeptides with 90%, 95%, or 97% identity to the amino acids of Ala (63) - Ser (208) of

SEQ ID NO:2, wherein said polypeptides stimulate proliferation of epithelial cells. Therefore, the specification contains an adequate written description of the claimed polypeptides. Accordingly, Applicants respectfully request that the Examiner's rejection of the claim 95-102 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

II. Double Patenting Rejection

a. The Examiner has rejected claims 95-102 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 83-86 of U.S. Patent 6,077,692. In particular, the Examiner alleges that the conflicting claims are not patentably distinct "since the patent and the application are claiming common subject matter, as follows: an isolated polypeptide comprising the amino acid sequence Ala(63) – Ser (208) of SEQ ID NO:2, and compositions thereof." *See*, paragraph spanning pages 4-5.

Although Applicants do not acquiesce to the instant rejection, in the interest of facilitating prosecution, Applicants have submitted a terminal disclaimer over U.S. Patent 6.077,692. Accordingly, Applicants respectfully request the Examiner to withdraw this rejection.

b. The Examiner has also provisionally rejected claims 95-102 under the judicially created doctrine of obvious-type double patenting over claims 189-200 of co-pending U.S. Application No. 09/345,373. In particular, the Examiner alleges that the subject matter encompassed by the '373 application "overlaps and encompass[es] identical and obvious embodiments" of the instant invention. *See,* page 5, paragraphs 2-3.

Without acquiescing to this rejection, Applicants note that this rejection should be the only rejection remaining in this application upon entry of the present amendment. Accordingly, pursuant to M.P.E.P. § 804, the rejection should be withdrawn and this case should proceed to issuance. Applicants will address the rejection, if necessary, in either the instant application or in the '373 application once either of the applications proceeds to issuance and the rejection is no longer provisional.

Applicants further note that a terminal disclaimer over the '692 patent was filed in the '373 application. Thus, both the '373 application and the instant invention have disclaimed any further patent term after the expiration of the '692 patent. Accordingly, no

further disclaimer should be needed and Applicants respectfully request the Examiner to withdraw this rejection.

Conclusion

Applicants respectfully request that the above-made remarks and amendments be entered and made of record in the file history of the instant application. In view of the foregoing remarks, Applicants believe that this application is now in condition for allowance, and an early notice to that effect is urged. The Examiner is invited to call the undersigned at the phone number provided below if any further action by Applicants would expedite the allowance of this application. If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136, such an extension is requested and the fee should also be charged to our Deposit Account.

Dated: July 15, 2004

Respectfully submitted,

By _____

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